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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,393	08/01/2003	Brian McKeown	13428-US	2918

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EXAMINER

WHALEY, PABLO S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 02/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/632,393	Applicant(s) MCKEOWN ET AL.	
	Examiner Pablo Whaley	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-61 is/are pending in the application.
- 4a) Of the above claim(s) 1-50 and 53-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 51 and 52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>10/21/05, 3/21/05</u> | 6) <input checked="" type="checkbox"/> Other: <u>IDS 10/20/04</u> |

DETAILED ACTION*APPLICANTS' ELECTION*

Applicants' election without traverse of Group III drawn to Claims 51 and 52 with traverse, filed 12/28/2005, is acknowledged. In response to applicants concerns regarding Claim 50, it is acknowledged that Claim 50 was intended to be a part of Group II, as it depends from Claim 49. In response to applicant's arguments, reasons for distinction between Groups I-V were stated in the previous office action. For example, Group V, although it recites a step of determining nucleotide identity as in claim 1, is drawn to a method of breeding sheep and thus was not included in Group I, which does not recite any limitations with regard to breeding animals. In general, Groups I-V are drawn to different methods which are not obvious variants. The burden of search is therefore maintained as the examination process requires a search of non-patent literature, U.S. patent publications, U.S. patents, as well as foreign patent literature. Claims 1-50 and 53-61 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/28/2005.

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 51 and 52.

OBJECTIONS

Claim 51 is objected to because of the following informalities: Claim 51 is grammatically incorrect, and should recite "incorporation of chain terminators at known ratios" in line 12. Appropriate correction is required.

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Claims 51 and 52 are objected to because of the following informalities: Claims 51 and 52 are grammatically incorrect, and should recite “polymorphisms of unknown ratios” in line 13 and line 4 respectively. Appropriate correction is required.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 recites a “method of monitoring the efficiency of incorporation” in the preamble. It is unclear in what way the steps of claim 51 achieve the purpose of the preamble, however, as Claim 51 results in “using the information...to interpret observed efficiencies.” Clarification is requested. Claim 52 is rejected as it depends from claim 51.

Claim 51 recites the phrase “thereby monitoring the efficiency of incorporation” in line 9. It is unclear what is meant by the term “monitoring”, as there is no such step of “monitoring” per se. Clarification is requested.

Claim 51 recites the limitation “population of primers at the known ratios” in line 9. There is insufficient antecedent basis for this limitation, as the only previous mention of known ratios referred to “amplicons comprising sequences at known ratios.” Furthermore, it is unclear if “known ratios” is referring to sequences, populations of primers, or both. Clarification is requested.

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Claim 52 recites the limitation "employed" in line 2. It is unclear if this is a physical step of the method as disclosed. It is further unclear in what way this limitation is related to "efficiency of incorporation." Clarification is requested.

Claims 51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 51 recites "efficiency of incorporation of chain terminators into primers" in the preamble. However, there is no step of "incorporating chain terminators into primers" in the instant claims. The omitted steps are between the step of "generating a population of amplicons" and "detecting and measuring efficiency of incorporation of chain terminators into the population of primers". Clarification is requested.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 51 and 52 are rejected under 35 U.S.C. 102 (b) as being anticipated by Pastinen et al. (Clinical Chemistry, 1996, 42:9, p.1391-1397).

Pastinen et al. teach multiplex, fluorescent, solid-phase mini-sequencing to detect multiple SNPs using fluorescent dideoxynucleotides (ddNTPs) (Abstract). More specifically, Pastinen et al. teach the following aspects of the instantly claimed invention:

- Performing PCR reactions using different HLA genes and known sequence specific primers [Table 1, and p.1392 "PCR Reactions" Section] and capturing PCR products (i.e. amplicons) [p.1392, col. 2, paragraph 3], which correlates to instant claim 51 (lines 3-4).
- Each primer used is of known concentrations [Table 1], which correlates to known ratios as in instant claim 51.
- Performing primer extension reactions on biotinylated PCR products (i.e. amplicons) employing ddNTP and minisequencing primers [Fig. 1, lines 1-9], which correlates to extension with chain terminators as in instant claim 51 (lines 5-7). Note: Specification teaches usage of dideoxynucleotides (i.e. ddNTPs) as chain terminators (p. 35, line 29).
- Incorporation of ddNTPs into primers [p.1394, col. 1, lines 1-4] and [Fig. 1, lines 16-20], which correlates to incorporation of chain terminators into primers as in instant claims 51 and 52.
- Detection of polymorphisms by detecting and measuring extended primers with electrophoresis [Fig. 1, lines 15-19], which correlates to measuring

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efficiency of incorporation of chain terminators into primers as in instant claim 51 (lines 8-10).

- Detection of primer codon ratios (A, C, G, and T) for different genotypes corresponding to respective dideoxynucleotides (i.e. chain terminators) for using in genotyping [Fig. 2 and Fig. 3],
- Optimized multiplex procedure using cell lines of known genotype by adjusting primer concentrations to increase ddNTP incorporation [p.1394, col. 1, paragraph 3].
- Using multiplex method above, correctly assigned the genotype of all blind samples containing point mutations [p.1394, col. 2, paragraph 2], which correlates to instant claim 51 (lines 11-13) and claim 52.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 51 and 52 are rejected under 35 U.S.C. 103(a) as being obvious by Van Ness et al. (Pub. Pat. US2004/0038256, Filed: Oct. 1, 2001), in view of Pastinen et al. (Clinical Chemistry, 1996, 42:9, p.1391-1397).

Van Ness et al. teach methods, kits and compositions for incorporation of fluorescence labeled nucleotides into an EcoN I digestion product, and identification of a nucleotide of interest in a target nucleic acid [0188]. More specifically, Van Ness et al. teach the following aspects of the instantly claimed invention:

- Human genomic DNA from 34 unrelated individuals (i.e. mixed samples of target nucleic acid) were amplified with multiple primers for a specific marker using PCR [0248], which correlates to instant claim 51 (lines 3-4).
- Performing primer extension on PCR product (i.e. amplicons) in the presence of allele-specific dye-labeled ddNTPs (i.e. chain terminators) [0252], as in instant claim 51 (lines 5-7).
- Primer extension products with known sequence ratios (i.e. numbers of A, T, G, C) [Fig. 6], as in instant claim 51.
- Oligonucleotide primers designed in relation to the target nucleic acid such that a 5' overhang may be filled in (i.e. extended) with fluorescence labeled nucleotides [189].
- detection of incorporated fluorescence labeled nucleotides with fluorescence polarization [0253], which correlates to instant claim 51 (lines 8-10).
- Software and algorithms for analysis of sequence information and measurement of intensity ratios derived from fluorescence polarization based on incorporated [0212], [0254], and [Fig. 2], which correlates to instant claim 51 (lines 8-10)

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- Methods by which the identity of the unknown nucleotide(s) (i.e. SNPs) becomes known [0140] and [0142].
- alkaline phosphatase to increase the efficiency of the incorporation of fluorescence labeled nucleotides [0190]

Van Ness et al. do not specifically teach the “efficiency of incorporation of chain terminators into primers” per se, but do suggest oligonucleotide primers may be extended with fluorescence labeled nucleotides [189], such as ddNTPs [Claim 65].

Pastinen et al. teach multiplex, fluorescent, solid-phase mini-sequencing to detect multiple SNPs using fluorescent dideoxynucleotides (ddNTPs) for primer extension [Abstract] and [p.1394, col. 1, lines 1-4], as previously discussed.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the invention of Van Ness et al. with the multiplex minisequencing system of Pastinen et al., where the motivation would have been to efficiently screen large numbers of samples for genetic disorders and interpret results automatically [Pastinen et al., p. 1396, col. 2, paragraph 1], resulting in the practice of the instant claimed invention with a reasonable expectation of success.

DOUBLE PATENTING

Claims 51 and 52 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 47 and 48 of copending Application No. #10/328,150. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

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CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
2/14/06

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